Hemoglobinopathies

The State Public Health Laboratory has been screening all infants for hemoglobinopathies since April of 1989. The Newborn Screening Laboratory uses a two-tiered screening system whereby all specimens are tested using Isoelectric Focusing (IEF), which is electrophoresis in a pH gradient. Any samples obtaining abnormal or questionable results are re-assayed using the next level of testing which is High Performance Liquid Chromatography (HPLC). These two methodologies are highly complimentary in sensitivity and specificity, detecting not only disease conditions, but also infants who are trait carriers. Parents of infants with abnormal traits are offered genetic counseling and no cost hemoglobin phenotype testing in order to ascertain if they are at risk for having children with hemoglobinopathy disease conditions in the future.

When a hemoglobinopathy condition is detected, the physician of record is notified by the 2nd or 3rd day after the specimen was received in the laboratory. Whole blood repeat testing on the infant and parents is advised to confirm the disease and aid in diagnosing the hemoglobinopathy. With sickle cell anemia, early detection is followed up by prophylactic antibiotic treatment, which greatly reduces deaths from bacteremia, pneumonia, and meningitis in these children. Hemoglobinopathy resource centers are available for parent counseling and continual observation of the child's health.

Hemoglobin Diseases

A group of autosomal recessive disorders characterized by synthesis of abnormal hemoglobin molecules (e.g. S, C, D, & E) or decreased synthesis of alpha or beta globin chains (thalassemia). For a hemoglobinopathy disease condition to exist, an abnormal hemoglobin or thalassemia typically must be inherited from both parents resulting in a homozygous or double heterozygous condition. The most common hemoglobinopathy in this country is Sickle Cell Disease. Infants with Sickle Cell Disease conditions often have early overwhelming sepsis and require prompt evaluation at a comprehensive care facility. Parents of these infants are referred to Hemoglobinopathy Resource Centers contracted by the Missouri Department of Health for treatment and follow-up care.

Prevalence (MO): 1:400 (Sickle cell disease in African-Americans)
1:3000 (General Population)

Analytes Measured: Hemoglobin Fractions
Fetal (F), Adult (A), Sickle (S), C-Hemoglobin (C),
E-Hemoglobin (E), D-Hemoglobin (D).

Reporting Ranges: FA = Normal
FS = Homozygous S or Sickle thalassemia
FSC = Sickle Hemoglobin-C disease
FSA = Sickle beta plus thalassemia
FSD = Sickle Hemoglobin-D disease
FSE = Sickle Hemoglobin-E disease
FC = Homozygous C or C - thalassemia
FCA = Hemoglobin-C beta plus thalassemia
FE = Homozygous E or E - thalassemia
FEA = Hemoglobin-E beta plus thalassemia
F only = Possible homozygous beta thalassemia

Feeding Effect: None

Timing Effect: None (unless transfusion is needed)

> **Note:** Sample collection after a transfusion with red blood cells invalidates hemoglobin test results for a minimum of 90 days post transfusion. It is recommended that a sample be collected prior to a transfusion, if at all possible. If a baby has been transfused prior to sample collection, note it on the collection form.

Confirmation: Whole blood repeat samples collected from the infant and both parents within two weeks. The Missouri State Lab can provide blood collection kit and no-cost testing.

Treatment: Prophylactic antibiotics

Common Hemoglobin Traits

A trait condition (carrier state) exists when a person inherits one normal hemoglobin gene and one abnormal gene. This person is healthy under normal circumstances and often is not aware they are carrying an abnormal hemoglobin. There is enough normal hemoglobin present to offset the dysfunction of the abnormal hemoglobin (there are some rare exceptions and extenuating circumstances where trait carriers can have symptoms). Like other recessive traits, hemoglobin traits may be passed along for many generations and not cause disease in offspring until which time they are inherited from both parents. Parents of infants who are found to have abnormal traits are offered hemoglobin phenotype testing by the state Laboratory and genetic counseling by the sickle cell program.

Prevelance: 1:12 (Sickle Cell trait in African-Americans)
1:30 (Hemoglobin C trait in African-Americans)
1:10 (Hemoglobin E trait in Southeast Asians)
1:10,000 (Hemoglobin D trait in Caucasians)

Analytes Measured: Hemoglobin Fractions
Fetal (F), Adult (A), Sickle (S), C-Hemoglobin (C), E-Hemoglobin (E), D-Hemoglobin (D).

Reporting Ranges: FA = Normal
FAS = Sickle Cell Trait
FAC = Hemoglobin C Trait
FAE = Hemoglobin E Trait
FAD = Hemoglobin D Trait

Feeding Effect: None

Timing Effect: None (unless transfusion is needed)

Confirmation: Recommend whole blood samples collected from parents to ascertain risk for having a future child with a hemoglobinopathy condition. The Missouri State Lab can provide blood collection kits and no-cost testing.

Treatment: None

Hemoglobin Variants

In the course of screening all newborns for the presence of the common abnormal hemoglobins, various other hemoglobin variants are uncovered, most of which are by and large unidentified. There are over 800 hemoglobin variants described in the literature at present. The vast majority of these have little known clinical ramifications and end up being merely incidental findings. Many are fetal hemoglobin variants that fade away with the fetal hemoglobin by six months of age and become undetectable. An exception to this is Bart's hemoglobin. The presence of Bart's hemoglobin is indicative of alpha thalassemia and can result in a mild microcytic anemia. A highly elevated Bart's hemoglobin may be clinically significant, especially in Southeast Asians.

Any concern for the rare symptomatic variant can be monitored through clinical observations (anemia, jaundice, cyanosis) combined with a CBC and reticulocyte count.

Parents of newborns found to have unidentified variants are offered hemoglobin phenotype testing free of charge by the State Laboratory.

Prevalence: 1:1000 (Approximation)

Analytes Measured: Hemoglobin Fractions

Fetal (F), Adult (A), Unidentified (X)

Reporting Ranges: FA = Normal

FAX = Unidentified Trait

Feeding Effect: None

Timing Effect: None (unless transfusion is needed)

Confirmation: Whole blood repeat testing on infant (at 4 months of age) and parents is offered. Missouri State Lab can provide blood collection kits and no-cost testing.

Treatment: None

Adult Screening Program

The adult testing program provides testing for parents who have obtained abnormal hemoglobinopathy screening results on their newborns. Since the screening of all Missouri's newborns for abnormal hemoglobins did not begin until 1989, many of these parents were unaware that they have an abnormal hemoglobin trait and could possibly be at risk for having a child with a disease condition in the future. The adult testing program also accepts whole blood samples for confirmation or further investigation of abnormal hemoglobinopathy test results obtained from other adult screening laboratories within the state.

Prevalence: 1:400 (Sickle Cell Disease in African-Americans)
1:3000 (General Population)

Analytes Measured: Hemoglobin Fractions:
Fetal (F), Adult (A & A2), Sickle (S), C-Hemoglobin (C), E-Hemoglobin (E), D-Hemoglobin (D), Unidentified

Hemoglobin (X).

Reporting Ranges:

A,A2 = Normal
A,S,A2 = Sickle Cell Trait
S,A,F,A2 = Sickle Beta Plus Thalassemia
S,F,A2 = Sickle Cell Disease or Sickle Thalassemia
A,C,A2 = Hemoglobin C Trait
C,A2 = Hemoglobin C Disease
S,C,A2 = Sickle Hemoglobin C Disease
A,X,A2 = Unidentified Hemoglobin Trait